



(1) providing a preparation containing a mammalian presenilin-1 protein, or a fragment, variant or mutant of said mammalian presenilin-1 protein that binds to said presenilin-1-interacting protein; a presenilin-1-interacting protein; and a candidate substance; and

(2) detecting whether said candidate substance affects said interaction of said presenilin-1-interacting protein with said mammalian presenilin-1 protein, or a fragment, variant or mutant of said mammalian presenilin-1 protein that binds to said presenilin-1-interacting protein.

The method of claim 10 of the instant application claims a method for identifying a candidate compound for treating a neuropsychiatric or neurodevelopmental disorder. The method comprises two steps:

(1) contacting a reconstituted system for measuring presenilin associated membrane protein (PAMP) activity, comprising a PAMP, or a functional fragment thereof, and a PAMP substrate, with a test compound, the PAMP comprising an amino acid sequence at least 90% identical to at least one amino acid sequence selected from the group consisting of SEQ ID NO:14, SEQ ID NO:16 and SEQ ID NO:18; and

(2) detecting a difference in PAMP activity in the presence of the compound compared PAMP activity in the absence of the compound, wherein a decrease in PAMP activity identifies the candidate compound.

Comparing claim 1 of the '143 patent and claim 10 of the instant application it is evident that there are differences between claim 1 of the '143 patent and claim 10 of the instant application (e.g., the use of PAMP or a functional fragment thereof, or identifying a candidate compound for treating a neurological disease) and that these differences would not have been obvious to one of ordinary skill for the following reasons:

Claim 1 of the '143 patent does not teach the use of a PAMP comprising an amino acid sequence at least 90% identical to at least one amino acid sequence selected from the group consisting of SEQ ID NO:14, SEQ ID NO:16 and SEQ ID NO:18, as recited in claim 10. Claim 1







Applicants submit that the present claims are clear and unambiguous and therefore respectfully request withdrawal of the rejection, in view of the present remarks.

*(c) Rejections Under 35 U.S.C. § 112, first paragraph*

The Examiner has further rejected claims 10, 11 and 17 through 23 for allegedly failing meet the written description requirement. Specifically, the Examiner maintains that the specification does not describe PAMP proteins having at least 90% identity to SEQ ID NO: 14, 16 or 18 as having the recited activity. Applicants respectfully traverse the present rejection.

Applicants specifically direct the Examiner to the definition of PAMP spanning page 8, line 17 through page 9, line 12. The definition of PAMP recited in the specification embraces not only the sequence recited in claim 1, but also derivatives and variants thereof. The definition includes, but is not limited to, PAMP having conserved structural features, relative to orthologues from *D. melanogaster* and *C. elegans*, both of which are clearly PAMP orthologs or homologs but have less than 90% sequence identity to PAMP. The definition further provides for naturally occurring variants, e.g., other mammalian PAMPs, allelic variants and mutant forms.

Not only have the applicants described the claimed invention with words, they have also provided a working example of several PAMP mutants falling within the scope of claim 1. Example 2 describes the use of eight distinct PAMP mutants in an experiment to evaluate the role of PAMP in the processing of  $\beta$ APP. The methods of Example 2 monitored the interaction of PAMP with a PAMP substrates and its effect on the processing of  $\beta$ APP to  $A\beta$  and exemplify PAMPs having all the limitations of claim 10. (Example 2, page 43, line 20 to page 45, line 25).

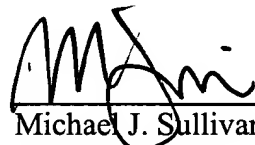
The applicants have provided both a detailed description of the invention and examples which demonstrates that the applicants were in possession of the claimed invention at the time the application was filed and therefore the present rejection is unwarranted and applicants respectfully request that it be withdrawn.

**CONCLUSIONS**

In view of the foregoing amendments and remarks, it is respectfully requested that the application be reconsidered and that all pending claims be allowed and the case passed to issue.

If there are any other issues remaining, which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'M. Sullivan', is written over a horizontal line.

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